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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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EXAMINER: MINNIFIELD,N

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 5-1-96

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) ~~18, 19, 37-39~~ 1-39 is/are pending in the application.

Of the above, claim(s) 1-17, 20-36 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 18, 19, 37-39 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

DETAILED ACTION

Response to Amendment

15. Applicants' amendment filed May 1, 1996 is acknowledged and has been entered. Claims 18, 19, 34, 37, and 38 have been amended. It is noted that claim 34 is drawn to a nonelected invention. New claim 39 has been added. Claims 18, 19, and 37-39 are now pending in the present application. All rejections have been withdrawn except those discussed below.

16. The text of the 35 U.S.C. Code not included in this Office Action can be found in the prior Office Action.

17. Applicant's election with traverse of Invention II in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the application is a PCT application and subject to requirements of unity of invention, not restriction requirement in accordance with 35 USC 121. This is not found persuasive because This is not found persuasive because the absence of lack of unity in a PCT application does not preclude the Examiner from requiring an election as long as the Invention comprises a product and methods of preparing and using the product, which the restriction has set forth.

It is noted that claim 34 was listed on Form 326 as being rejected however this was incorrect. Claim 34 should be included in Invention III as previously set forth in the Restriction Requirement.

The requirement is still deemed proper and is therefore made FINAL.

18. This application contains claims 1-17 and 20-36 drawn to an invention non-elected with traverse in Paper No. 10. A complete response to the final rejection must include cancellation of

non-elected claims or other appropriate action (37 CFR 1.144) MPEP § 821.01.

19. The objection to the specification and rejection of claims 37 and 38 under 35 U.S.C. § 112, first paragraph (i.e. lack of an enabling disclosure) is maintained. This rejection is maintained for essentially the same reasons as the rejection of claims 37 and 38 under this statutory provision, as set forth in the last Office action. Applicants' arguments filed May 1, 1996, have been fully considered but they are not deemed to be persuasive.

The following is a quotation of the first paragraph of 35 U.S.C. § 112: The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure. The claims, 37 and 38, are directed to antibodies, and compositions to treat infection due to *H. pylori*. However, the specification is not enabled for nor has taught one of skill in the art how to obtain these antibodies and compositions to treat infection due to *H. pylori*. It is noted that the art teaches that "[W]ith the exception of UreA and UreB structural polypeptides of the enzyme, no role can as yet be assigned to the nine proteins encoded by the *H. pylori* urease gene cluster." (Cussac et al. 1992, abstract). Therefore it is unclear how the products, polypeptides, from these genes can be used in compositions to treat infection due to *H. pylori*. Further, Houghten et al. teach that changes/ modifications (addition, substitution, deletion or inversion) of one or more amino acids in a polypeptide will alter antigenic determinants and therefore effect antibody production (p. 21). Houghten et al. also teach that "... combined effects of multiple changes in an antigenic determinant could result in a loss of [immunological] protection." and "A protein having

multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies..." (p. 24). It is not always possible to make antibodies or protect against infection if the antigenic determinants have been altered. Applicants propose to make recombinant strains using mutations in the Ure genes and then use these in compositions, however as set forth above it is unclear if changes/modifications that occur in the gene will effect the antigenic determinants; i.e. are the determinants maintained in order to obtain a composition. Further, the antigenic determinants or epitopes have not been disclosed for the *H. pylori* urease. The specification has not taught the use of fragments; how to obtain these fragment or how much of the polypeptide constitutes a fragment. What is the minimal portion that is needed for the polypeptide to remain functional? In view of the reasons set forth, there would be undue experimentation for a skilled artisan to practice the claimed invention.

Applicants have asserted that the present specification provides antibodies and polypeptides that provide therapeutic benefits. However, it is noted that there is no known function of the presently claimed polypeptides that Applicants used for the antibody preparation and polypeptides claimed to treat infection due to *H. pylori*. The primary claims (18 and 19) recite that the polypeptides can have modifications and as taught by Houghten these modifications can change or alter antigenic determinants and therefore effect antibody production (p. 21). Houghten et al. also teach that "... combined effects of multiple changes in an antigenic determinant could result in a loss of [immunological] protection." and "A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies..." (p. 24). It is not always possible to make antibodies or protect against infection if the antigenic determinants have been altered.

21. Claims 18, 19, 37 and 38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is maintained for essentially the same reasons as set forth in the last Office action. Applicant's arguments filed May 1, 1996 have been fully considered but they are not persuasive.

The claims are rejected as failing to define the invention in the manner required by 35 U.S.C. § 112, second paragraph. The claims are narrative in form and replete with indefinite and functional or operational language. The structure which goes to make up the device must be clearly and positively specified. The structure must be organized and correlated in such a manner as to present a complete operative device. The claims must be in one sentence form only. Note the format of the claims in the patent cited (Rashtchian et al.). The claims are indefinite for being in improper Markush format. The Office recommends the use of the phrase "selected from the group consisting of..." with the use of the conjunction "and" rather than "or" in listing the species. See MPEP 706.03(Y). The use of the phrase "for example" renders claim 18 indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention or not, and the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The phrase "such as" renders the claim 19 indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention or not, and the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Claim 38 lacks positive antecedent basis in the recitation of "antibody".

Claim 38 now refers to "polyclonal or monoclonal antibody", which lacks antecedent basis.

Applicants refer to attenuated activity and Fragment 209-282, however it is unclear what Applicants mean as these limitations are not set forth in the claims.

22. The rejection of claims 18, 19, and 39 under 35 U.S.C. § 102(b) as anticipated by, or in the alternative, under 35 U.S.C. § 103 as obvious over Mulrooney et al., Bradley et al. or Tabaqchali et al. is maintained. This rejection is maintained for essentially the same reasons as the rejection of claims 18 and 19 under this statutory provision, as set forth in the last Office action. Applicants' arguments filed May 1, 1996 , have been fully considered but they are not deemed to be persuasive.

Mulrooney et al. disclose polypeptides encoded by the UreE, UreF and UreG (abstract). Mulrooney et al. disclose that these genes are accessory genes in urease activity (abstract; p. 5839). Bradley et al. disclose Ure genes, UreE and UreF, that encode for polypeptides (abstract; materials and methods). Tabaqchali et al. disclose nucleotide sequences characterized in that it comprises a part of the nucleic sequence (2622-2693) corresponding to the gene known as UreI.

The prior art, Mulrooney et al., Bradley et al. or Tabaqchali et al., discloses polypeptides, which appears to be the same as the claimed invention. Therefore, the prior art polypeptides appear to be the same, with any other identifying characteristics inherent in them. The art anticipates the claimed invention because the claims recite any part of the claimed sequence; it covers virtually any portion of the amino acid sequence.

And if the prior art products, polypeptides, are not the same as that claimed, they are obvious variations of that claimed, which the teachings of the prior art would have reasonably suggested to one of ordinary skill in the art at the time the invention was made, to use the disclosed genes to express the claimed polypeptides, making the claimed invention, as a whole prima facie obvious to one of ordinary skill in the art at the time the invention was made. It would have been obvious to a person of ordinary skill in the art at the time the invention was made that the polypeptide corresponding to the sequence disclosed in the art can easily be derived.

Since the Office does not have the facilities for examining and comparing applicants' disclosed polypeptides and the disclosed polypeptides of the prior art the burden is on applicant to

show a novel or unobvious differences between the claimed polypeptide and the disclosed polypeptides of the prior art (i.e., that the disclosed polypeptides of the prior art does not possess the same material structural and functional characteristics of the claimed polypeptides). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants have asserted that the prior art source was not *H. pylori* and that the sequences are not the same. However, the claims recite the Ure polypeptides disclosed in the art. The source of the polypeptides is not recited in the claims, and further the claims recite "any part of at least one of its polypeptide."

23. The following new ground of rejection is set forth:

Claims 18, 19 and 39 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Ferrero et al..

It is noted that the authorship is not the same as the inventive entity and that it is unclear exactly when this reference was published.

Ferrero et al. disclose Ure genes from *H. pylori* and the expression of these genes in *C. Jejuni* or *E. Coli* (abstract).

The prior art, Ferrero et al., discloses polypeptides, which appears to be the same as the claimed invention. Therefore, the prior art polypeptides appear to be the same, with any other identifying characteristics inherent in them. The art anticipates the claimed invention because the claims recite any part of the claimed sequence; it covers virtually any portion of the amino acid sequence.

And if the prior art products, polypeptides, are not the same as that claimed, they are obvious variations of that claimed, which the teachings of the prior art would have reasonably suggested to one of ordinary skill in the art at the time the invention was made, to use the disclosed genes to express the claimed polypeptides, making the claimed invention, as a whole

prima facie obvious to one of ordinary skill in the art at the time the invention was made. It would have been obvious to a person of ordinary skill in the art at the time the invention was made that the polypeptide corresponding to the sequence disclosed in the art can easily be derived.

Since the Office does not have the facilities for examining and comparing applicants' disclosed polypeptides and the disclosed polypeptides of the prior art the burden is on applicant to show a novel or unobvious differences between the claimed polypeptide and the disclosed polypeptides of the prior art (i.e., that the disclosed polypeptides of the prior art does not possess the same material structural and functional characteristics of the claimed polypeptides). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

24. The rejection of claims 37 and 38 under 35 U.S.C. § 103 as obvious over Mulrooney et al., Ferrero et al., Bradley et al. or Tabaqchali et al. as applied to claims 18 and 19 above, and further in view of Sevier et al. is maintained. This rejection is maintained for essentially the same reasons as the rejection of claims 37 and 38 under this statutory provision, as set forth in the last Office action. Applicants' arguments filed May 1, 1996, have been fully considered but they are not deemed to be persuasive.

Mulrooney et al. disclose polypeptides encoded by the UreE, UreF and UreG (abstract). Mulrooney et al. disclose that these genes are accessory genes in urease activity (abstract; p. 5839). Bradley et al. disclose Ure genes, UreE and UreF, that encode for polypeptides (abstract; materials and methods). Tabaqchali et al. disclose nucleotide sequences characterized in that it comprises a part of the nucleic sequence (2622-2693) corresponding to the gene known as UreI. Sevier et al. teach the use of antibodies for immunodiagnositics or immunotherapy (abstract; p. 1800; 1802). It would have been obvious to a person of ordinary skill in the art the time the invention was made to use the polypeptides as taught in the prior art with the expectation of obtaining antibodies to the claimed polypeptides. Further, it would have been obvious to a person

of ordinary skill in the art at the time the invention was made to use the polypeptides in a composition to treat infection due to *H. pylori* since Ferrero et al. teach that these polypeptides can "...be useful in animal model for addressing the role of urease in the establishment and the maintenance of *H. pylori* infection." (abstract). The claimed invention is prima facie obvious in view of the teachings of Mulrooney et al., Bradley et al. or Tabaqchali et al. taken with Sevier et al., absent any convincing evidence to the contrary.

It is noted that the above 103 rejection is set forth for claims 37 and 38, not claims 18 and 19. Further, Ferrero et al. suggests that these polypeptides can be used for treatment of *H. pylori* infection.

25. The following new grounds of rejection have been necessitated by Applicants' amendment to the claims.

26. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification does not provide support for the recitation of a "pharmaceutical carrier" and "essentially purified and isolated".

27. No claims are allowed.

28. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is

reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is (703) 305-3394. The examiner can normally be reached on Monday-Thursday from 7:00 AM-4:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

N. M. Minnifield

August 22, 1996

James C. Housel

JAMES C. HOUSEL 9/3/96

SUPERVISORY PATENT EXAMINER

GROUP 180